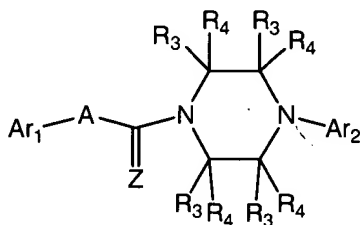


In the claims:

Cancel claims 1-3, 7, 24, 86, 87, 177-192, and 194-196.

Please enter amended claims 4, 5, 8, 9, 26, 27, 31, 32, 37, 40, 42, 44, 46, 48, 59, 62, 63, 161, and 169 as follows:

4. (Amended) A compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

A is absent or is selected from the group consisting of O, S,

NR_A, NR_ACR_BR_B, CR_BR_B'NR_A,

-CR_A=CR_B-, and C₃H₄; where R_A, R_B, and R_B' are independently selected at each occurrence from hydrogen and alkyl;

Z is oxygen or sulfur;

each R₃ and R₄ is independently

(a) selected from the group consisting of hydrogen;

halogen; hydroxy; amino; cyano; nitro;

-COOH; -CHO; optionally substituted alkyl; optionally substituted alkenyl; optionally substituted alkynyl;

optionally substituted alkoxy; optionally substituted mono or dialkylamino; optionally substituted alkylthio;

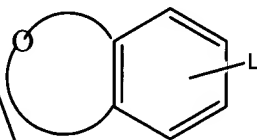
optionally substituted alkyl ketone; optionally substituted alkylester; optionally substituted alkylsulfinyl;

optionally substituted alkylsulfonyl; optionally substituted mono- or di-alkylcarboxamide; optionally substituted $-S(O)_nNHalkyl$; optionally substituted $-S(O)_nN(alkyl)(alkyl)$; optionally substituted $-NHC(=O)alkyl$; optionally substituted $-NC(=O)(alkyl)(alkyl)$; optionally substituted $-NHS(O)_nalkyl$; optionally substituted $-NS(O)_n(alkyl)(alkyl)$; optionally substituted saturated or partially unsaturated heterocycle of from 5 to 8 atoms, which saturated or partially unsaturated heterocycle contains 1, 2, or 3 heteroatoms independently selected from N, O, and S; optionally substituted aryl having from 1 to 3 rings; and optionally substituted heteroaryl, said heteroaryl having from 1 to 3 rings, 5 to 8 ring members in each ring and, in at least one of said rings, from 1 to about 3 heteroatoms per ring independently selected from the group consisting of N, O, and S; or

- (b) joined to a R_3 or R_4 not attached to the same carbon to form an optionally substituted aryl ring, a saturated or partially unsaturated carbocyclic ring of from 5 to 8 members, which carbocyclic ring is optionally substituted, or a saturated, partially unsaturated, or aromatic heterocyclic ring of from 5 to 8 members, which heterocyclic ring is optionally substituted and contains 1, 2, or 3 heteroatoms selected from N, O, and S;

Ar₁ is selected from the group consisting of:

- (a) cyclohexyl, cyclopentyl, piperidiny1, piperaziny1, phenyl, pyrroly1, furanyl, thienyl, pyrazoly1, imidazoly1, thiazoly1, isothiazoly1, oxazoly1, isoxazoly1, oxadiazoly1, triazoly1, tetrazoly1, pyridyl, pyrimidyl, pyraziny1, benzimidazoly1, naphthyl, indoly1, isoindoly1, benzofuranyl, isobenzofuranyl, benzo[b]thiophenyl, benz[d]isoxazoly1, quinoliny1, isoquinoliny1, cinnoliny1, quinazoliny1, and quinoxaliny1, each of which is optionally mono-, di-, or trisubstituted with R₅; and
- (b) bicyclic oxygen-containing groups of the formula:



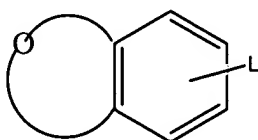
optionally mono-, di-, or trisubstituted with R₅, where L represents point of attachment and may be at any point on the benzene ring, and the oxygen-containing ring of the bicyclic oxygen-containing group consists of from 5 to 8 ring atoms, contains 1 or 2 oxygen atoms and remaining ring atoms are carbon;

Ar₂ is selected from the group consisting of:

- (a) cyclohexyl, cyclopentyl, piperidiny1, piperaziny1, pyrroly1, furanyl, thienyl, pyrazoly1, imidazoly1, thiazoly1, isothiazoly1, oxazoly1, isoxazoly1, oxadiazoly1,

triazolyl, tetrazolyl, pyridyl, pyrimidyl, pyrazinyl,
benzimidazolyl, naphthyl, indolyl, isoindolyl,
benzofuranyl, isobenzofuranyl, benzo[b]thiophenyl,
benz[d]isoxazolyl, quinolinyl, isoquinolinyl, cinnolinyl,
quinazolinyl, and quinoxalinyl, each of which is optionally
mono-, di-, or trisubstituted with R₅; and

(b) bicyclic oxygen-containing groups of the formula:



optionally mono-, di-, or trisubstituted with R₅, where L
represents point of attachment and may be at any point on
the benzene ring, and the oxygen-containing ring of the
bicyclic oxygen-containing group consists of from 5 to 8
ring atoms, contains 1 or 2 oxygen atoms and remaining ring
atoms are carbon;

R₅ is independently selected at each occurrence from the group
consisting of halogen, nitro, halo(C₁₋₆)alkyl, halo(C₁₋
6)alkoxy, hydroxy, amino, C₁₋₆alkyl substituted with 0-2 R₆,
C₂₋₆alkenyl substituted with 0-2 R₆, C₂₋₆alkynyl substituted
with 0-2 R₆, C₁₋₆alkoxy and Y;

R₆ is independently selected at each occurrence from the group
consisting of halogen, hydroxy, cyano, C₁₋₄alkyl, C₁₋₄alkoxy,
-S(O)_n(C₁₋₄alkyl), halo(C₁₋₄)alkyl, halo(C₁₋₄)alkoxy, CO(C₁₋

alkyl), CONH(C₁₋₄alkyl), CON(C₁₋₄alkyl₁)(C₁₋₄alkyl₂) where alkyl₁ and alkyl₂ may be joined to form a heterocycle of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms independently selected from N, O, and S, -XR₇, and Y;

X is independently selected at each occurrence from the group consisting of -CH₂-, -CHR₈-, -O-, -S(O)_n-, -NH-, -NR₈-, -C(=O)-, -C(=O)O-, -C(=O)NH-, -C(=O)NR₈-, -S(O)_nNH-, -S(O)_nNR₈-, NHC(=O)-, -NR₈C(=O)-, -NHS(O)_n-, and -NR₈S(O)_n-;

R₇ and R₈ are independently selected at each occurrence from hydrogen, and straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups, said straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups consisting of 1 to 8 carbon atoms, and containing zero or one or more double or triple bonds, each of which 1 to 8 carbon atoms is unsubstituted or substituted with one or more substituent(s) independently selected from oxo, hydroxy, halogen, amino, cyano, nitro, haloalkyl, haloalkoxy, -O(alkyl), -NH(alkyl), -N(alkyl)(alkyl), -NHC(O)(alkyl), -N(alkyl)C(O)(alkyl), -NHS(O)_n(alkyl), -S(O)_n(alkyl), -S(O)_nNH(alkyl), -S(O)_nN(alkyl₃)(alkyl₄) where alkyl₃ and alkyl₄ are optionally joined to form a heterocycle consisting of from 5 to 8 ring atoms and

containing 1, 2, or 3 heteroatoms independently selected from N, O, and S, and Y';

Y and Y' are independently selected at each occurrence from 3- to 8-membered carbocyclic or heterocyclic groups which are saturated, unsaturated, or aromatic, which may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, nitro, cyano, alkyl, alkoxy, haloalkyl, haloalkoxy, mono- or dialkylamino, and alkylthio;

wherein said 3- to 8-membered heterocyclic groups contain one or more heteroatom(s) independently selected from N, O, and S; and

n is independently chosen at each occurrence from 0, 1, and 2.

5. (Amended) A compound or salt according to Claim 4, wherein:

R_A, R_B, and R_B' are independently selected at each occurrence from hydrogen and C₁₋₆alkyl;

each R₃ and R₄ is independently

(a) chosen from the group consisting of hydrogen, halogen, cyano, nitro, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, hydroxy, amino, C₁₋₆alkyl substituted with 0-2 R₆, C₂₋₆alkenyl substituted with 0-2 R₆; C₂₋₆alkynyl substituted with 0-2 R₆; C₁₋₆alkoxy substituted with 0-2 R₆, -NH(C₁₋₆alkyl) substituted

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with 0-2 R₆, -N(C₁₋₆alkyl)(C₁₋₆alkyl) where each C₁₋₆alkyl is independently substituted with 0-2 R₆, -XR₇, and Y; or

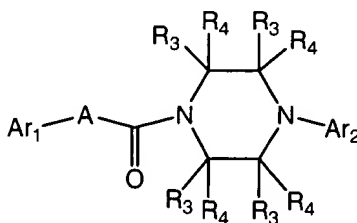
(b) joined to a R₃ or R₄ not attached to the same carbon to form an aryl ring substituted with 0-3 R₆, a saturated or partially unsaturated carbocyclic ring of from 5 to 8 members, which carbocyclic ring is substituted with 0-2 R₆, or a saturated, partially unsaturated, or aromatic heterocyclic ring of from 5 to 8 members, which heterocyclic ring is substituted with 0-2 R₆ and contains 1, 2, or 3 heteroatoms independently selected from N, O, and S;

R₇ and R₈ are independently selected at each occurrence from hydrogen, and straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups, said straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups consisting of 1 to 8 carbon atoms, and containing zero or one or more double or triple bonds, each of which 1 to 8 carbon atoms is unsubstituted or substituted with one or more substituent(s) independently selected from oxo, hydroxy, halogen, amino, cyano, nitro, haloalkyl, haloalkoxy, -O(alkyl), -NH(alkyl), -N(alkyl)(alkyl), -NHC(O)(C₁₋₄alkyl), -N(C₁₋₄alkyl)C(O)(C₁₋₄alkyl), -NHS(O)_n(C₁₋₄alkyl), -S(O)_n(C₁₋₄alkyl), -S(O)_nNH(C₁₋₄alkyl), -S(O)_nN(C₁₋₄alkyl)₃(C₁₋₄alkyl)₄ where C₁₋₄alkyl₃ and C₁₋₄alkyl₄ are

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optionally joined to form a heterocycle consisting of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms independently selected from N, O, and S, and Y'; and Y and Y' are independently selected at each occurrence from 3- to 8-membered carbocyclic or heterocyclic groups which are saturated, unsaturated, or aromatic, which are unsubstituted or substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, nitro, cyano, C₁₋₄alkyl, C₁₋₄alkoxy, halo(C₁₋₄)alkyl, halo(C₁₋₄)alkoxy, mono- or di(C₁₋₄)alkylamino, and C₁₋₄alkylthio; wherein said 3- to 8-membered heterocyclic groups contain one or more heteroatom(s) independently selected from N, O, and S.

8. (Amended) A compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

A is absent or is selected from the group consisting of O, S, NR_A, CR_BR_{B'}, NR_ACR_BR_{B'}, CR_BR_{B'}NR_A, -CR_A=CR_B-, and C₃H₄; where R_A, R_B, and R_{B'} are independently selected at each occurrence from hydrogen or alkyl; each R₃ and R₄ is independently

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(a) selected from the group consisting of hydrogen; halogen; hydroxy; amino; cyano; nitro; -COOH; -CHO, optionally substituted alkyl; optionally substituted alkenyl; optionally substituted alkynyl; optionally substituted alkoxy; optionally substituted mono or dialkylamino; optionally substituted alkylthio; optionally substituted alkyl ketone; optionally substituted alkylester; optionally substituted alkylsulfinyl; optionally substituted alkylsulfonyl; optionally substituted mono- or di-alkylcarboxamide; optionally substituted $-S(O)_nNHalkyl$; optionally substituted $-S(O)_nN(alkyl)(alkyl)$; optionally substituted $-NHC(=O)alkyl$; optionally substituted $-NC(=O)(alkyl)(alkyl)$; optionally substituted $-NHS(O)_nalkyl$; optionally substituted $-NS(O)_n(alkyl)(alkyl)$; optionally substituted saturated or partially unsaturated heterocycle of from 5 to 8 atoms, which saturated or partially unsaturated heterocycle contains 1, 2, or 3 heteroatoms independently selected from N, O, and S; optionally substituted aryl having from 1 to 3 rings; and optionally substituted heteroaryl, said heteroaryl having from 1 to 3 rings, 5 to 8 ring members in each ring and, in at least one of said rings, from 1 to about 3 heteroatoms per ring independently selected from the group consisting of N, O, and S; or

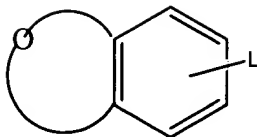
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(b) joined to a R_3 or R_4 not attached to the same carbon to form an optionally substituted aryl ring; a saturated or partially unsaturated carbocyclic ring of from 5 to 8 members, which carbocyclic ring is optionally substituted; or a saturated, partially unsaturated, or aromatic heterocyclic ring of from 5 to 8 members, which heterocyclic ring is optionally substituted and contains 1, 2, or 3 heteroatoms independently selected from N, O, and S;

Ar_1 and Ar_2 are independently selected from the group consisting of:

(a) cyclohexyl, cyclopentyl, piperidinyl, piperazinyl, pyrrolyl, furanyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, pyrimidyl, pyrazinyl, benzimidazolyl, naphthyl, indolyl, isoindolyl, benzofuranyl, isobenzofuranyl, benzo[b]thiophenyl, benz[d]isoxazolyl, quinolinyl, isoquinolinyl, cinnolinyl, quinazolinyl, and quinoxalinyl; wherein Ar_1 is optionally mono-, di-, or trisubstituted with R_5 , and Ar_2 is optionally mono-, di-, or trisubstituted with R_9 ; and

(b) groups of the formula:



optionally mono-, di-, or trisubstituted with R_5 , where L represents point of attachment and may be at any point on the benzene ring, and the oxygen-containing ring of the bicyclic oxygen-containing group consists of from 5 to 8 ring atoms, contains 1 or 2 oxygen atoms and remaining ring atoms are carbon;

R_5 is independently selected at each occurrence from the group consisting of cyano, nitro, haloalkyl, haloalkoxy, hydroxy, amino, alkyl substituted with 0-2 R_6 , alkenyl substituted with 0-2 R_6 , alkynyl substituted with 0-2 R_6 , alkoxy and Y;

R_9 is independently selected at each occurrence from the group consisting of nitro, haloalkoxy, hydroxy, amino, alkyl substituted with 0-2 R_6 , alkenyl substituted with 0-2 R_6 , alkynyl substituted with 0-2 R_6 , alkoxy substituted with 0-2 R_6 , and Y;

R_6 is independently selected at each occurrence from the group consisting of halogen, hydroxy, cyano, alkyl, alkoxy, - $S(O)_n$ (alkyl), haloalkyl, haloalkoxy, CO (alkyl), $CONH$ (alkyl), $CON(alkyl_1)(alkyl_2)$ where $alkyl_1$ and $alkyl_2$ may be joined to form a heterocycle of from 5 to 8 ring atoms and containing

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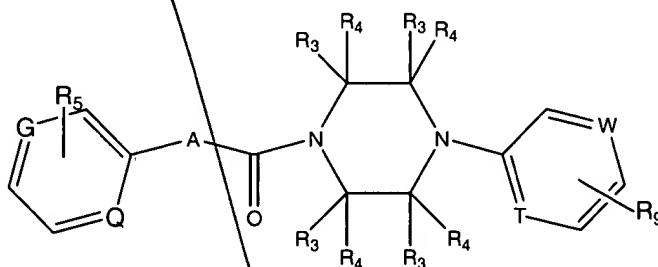
1, 2, or 3 heteroatoms independently selected from N, O, and S, -XR₇, and Y;

X is independently selected at each occurrence from the group consisting of -CH₂-, -CHR₈-, -O-, -S(O)_n-, -NH-, -NR₈-, -C(=O)-, -C(=O)O-, -C(=O)NH-, -C(=O)NR₈-, -S(O)_nNH-, -S(O)_nNR₈-, NHC(=O)-, -NR₈C(=O)-, -NHS(O)_n-, and -NR₈S(O)_n-;

R₇ and R₈ are independently selected at each occurrence from hydrogen, and straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups, said straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups consisting of 1 to 8 carbon atoms, and containing zero or one or more double or triple bonds, each of which 1 to 8 carbon atoms is unsubstituted or substituted with one or more substituent(s) independently selected from oxo, hydroxy, halogen, amino, cyano, nitro, haloalkyl, haloalkoxy, -O(alkyl), -NH(alkyl), -N(alkyl)(alkyl), -NHC(O)(alkyl), -N(alkyl)C(O)(alkyl), -NHS(O)_n(alkyl), -S(O)_n(alkyl), -S(O)_nNH(alkyl), -S(O)_nN(alkyl₃)(alkyl₄) where alkyl₃ and alkyl₄ are optionally joined to form a heterocycle consisting of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms independently selected from N, O, and S, and Y';

Y and Y' are independently selected at each occurrence from 3-
 to 8-membered carbocyclic or heterocyclic groups which are
 saturated, unsaturated, or aromatic, which are
 unsubstituted or substituted with one or more substituents
 independently selected from halogen, oxo, hydroxy, amino,
 nitro, cyano, alkyl, alkoxy, haloalkyl, haloalkoxy, mono-
 or dialkylamino, and alkylthio;
 wherein said 3- to 8-membered heterocyclic groups contain one
 or more heteroatom(s) independently selected from N, O, and S;
 and
 n is independently chosen at each occurrence from 0, 1, and 2.

9. (Amended) A compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

G, Q, T, and W are the same or different and are selected from
 the group consisting of N, CH, and CR₅, wherein T or W or
 both is N;

A is absent or is selected from the group consisting of O, S,
 NR_A, CR_BR_B', NR_ACR_BR_B', CR_B R_B'NR_A, -CR_A=CR_B-, and C₃H₄; where

R_A , R_B , and R_B' are independently selected at each occurrence from hydrogen and alkyl;

Z is oxygen or sulfur;

each R_3 and R_4 is independently

- (a) selected from the group consisting of hydrogen; halogen; hydroxy; amino; cyano; nitro; -COOH; -CHO, optionally substituted C_{1-6} alkyl; optionally substituted C_{2-6} alkenyl; optionally substituted C_{2-6} alkynyl; optionally substituted C_{1-6} alkoxy; optionally substituted mono or di(C_{1-6})alkylamino; optionally substituted C_{1-6} alkylthio; optionally substituted C_{1-6} alkyl ketone; optionally substituted C_{1-6} alkylester; optionally substituted C_{1-6} alkylsulfinyl; optionally substituted C_{1-6} alkylsulfonyl; optionally substituted mono- or di(C_{1-6})alkylcarboxamide; optionally substituted $-S(O)_nNH$ C_{1-6} alkyl; optionally substituted $-S(O)_nN(C_{1-6}alkyl)(C_{1-6}alkyl)$; optionally substituted $-NHC(=O)$ C_{1-6} alkyl; optionally substituted $-NC(=O)(C_{1-6}alkyl)(C_{1-6}alkyl)$; optionally substituted $-NHS(O)_nC_{1-6}alkyl$; optionally substituted $-NS(O)_n(C_{1-6}alkyl)(C_{1-6}alkyl)$; optionally substituted saturated or partially unsaturated heterocycle of from 5 to 8 atoms, which saturated or partially unsaturated heterocycle contains 1, 2, or 3 heteroatoms independently selected from N, O, and S; optionally substituted aryl having from 1 to 3

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rings; and optionally substituted heteroaryl, said heteroaryl having from 1 to 3 rings, 5 to 8 ring members in each ring and, in at least one of said rings, from 1 to about 3 heteroatoms per ring independently selected from the group consisting of N, O, and S; or

- (b) joined to a R₃ or R₄ not attached to the same carbon to form an optionally substituted aryl ring; a saturated or partially unsaturated carbocyclic ring of from 5 to 8 members, which carbocyclic ring is optionally substituted; or a saturated, partially unsaturated, or aromatic heterocyclic ring of from 5 to 8 members, which heterocyclic ring is optionally substituted and contains 1, 2, or 3 heteroatoms independently selected from N, O, and S;

R₅ represents 1 to 3 substituents independently selected at each occurrence from the group consisting of cyano, hydroxy, amino, C₃₋₆ alkyl substituted with 0-2 R₆, C₂₋₆ alkenyl substituted with 0-2 R₆, C₂₋₆ alkynyl substituted with 0-2 R₆, C₃₋₆ alkoxy, -NH(C₁₋₆alkyl) substituted with 0-2 R₆, -N(C₁₋₆alkyl)(C₁₋₆alkyl) where each alkyl is independently substituted with 0-2 R₆, -XR₇, and Y;

R₉ represents 0 to 3 substituents independently selected at each occurrence from the group consisting of halogen, nitro, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, hydroxy, amino, C₁₋₆alkyl

substituted with 0-2 R_6 , C_{2-6} alkenyl substituted with 0-2 R_6 , C_{2-6} alkynyl substituted with 0-2 R_6 , C_{1-6} alkoxy substituted with 0-2 R_6 , and Y;

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 R_6 is independently selected at each occurrence from the group consisting of halogen, hydroxy, cyano, C_{1-4} alkyl, C_{1-4} alkoxy, $-S(O)_n(C_{1-4}alkyl)$, halo(C_{1-4})alkyl, halo(C_{1-4})alkoxy, $CO(C_{1-4}alkyl)$, $CONH(C_{1-4}alkyl)$, $CON(C_{1-4}alkyl_1)(C_{1-4}alkyl_2)$ where $alkyl_1$ and $alkyl_2$ may be joined to form a heterocycle of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms independently selected from N, O, and S, $-XR_7$, and Y;

X is independently selected at each occurrence from the group consisting of $-CH_2-$, $-CHR_8-$, $-O-$, $-S(O)_n-$, $-NH-$, $-NR_8-$, $-C(=O)-$, $-C(=O)O-$, $-C(=O)NH-$, $-C(=O)NR_8-$, $-S(O)_nNH-$, $-S(O)_nNR_8-$, $NHC(=O)-$, $-NR_8C(=O)-$, $-NHS(O)_n-$, and $-NR_8S(O)_n-$;

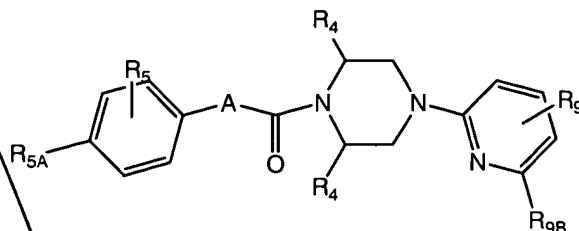
R_7 and R_8 are independently selected at each occurrence from hydrogen, and straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups, said straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups consisting of 1 to 8 carbon atoms, and containing zero or one or more double or triple bonds, each of which 1 to 8 carbon atoms is unsubstituted or substituted with one or more substituent(s) independently selected from oxo,

hydroxy, halogen, amino, cyano, nitro, haloalkyl,
haloalkoxy, $-O(C_{1-4}alkyl)$,
 $-NH(C_{1-4}alkyl)$, $-N(C_{1-4}alkyl)(C_{1-4}alkyl)$, $-NHC(O)(C_{1-4}alkyl)$, $-$
 $N(C_{1-4}alkyl)C(O)(C_{1-4}alkyl)$, $-NHS(O)_n(C_{1-4}alkyl)$, $-S(O)_n(C_{1-4}alkyl)$, $-S(O)_nNH(C_{1-4}alkyl)$, $-S(O)_nN(C_{1-4}alkyl_3)(C_{1-4}alkyl_4)$
where $C_{1-4}alkyl_3$ and $C_{1-4}alkyl_4$ are optionally joined to form
a heterocycle consisting of from 5 to 8 ring atoms and
containing 1, 2, or 3 heteroatoms independently selected
from N, O, and S, and Y';

Y and Y' are independently selected at each occurrence from 3-
to 8-membered carbocyclic or heterocyclic groups which are
saturated, unsaturated, or aromatic, which are
unsubstituted or substituted with one or more substituents
independently selected from halogen, oxo, hydroxy, amino,
nitro, cyano, $C_{1-4}alkyl$, $C_{1-4}alkoxy$, $halo(C_{1-4})alkyl$, $halo(C_{1-4})alkoxy$,
mono- or di(C_{1-4})alkylamino, and $C_{1-4}alkylthio$;
wherein said 3- to 8-membered heterocyclic groups contain
one or more heteroatom(s) independently selected from N, O,
and S; and

n is independently chosen at each occurrence from 0, 1, and 2.

26. (Amended) A compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

A is selected from the group consisting of NH, -CH=CH-, and CH₂NH;

R₄ is independently chosen from hydrogen and C₁₋₄ alkyl;

R₅ represents 0 to 2 substituents independently chosen at each occurrence from the group consisting of halogen, cyano, nitro, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, hydroxy, amino, C₁₋₆alkyl substituted with 0-2 R₆, C₂₋₆alkenyl substituted with 0-2 R₆, C₂₋₆alkynyl substituted with 0-2 R₆, C₁₋₆alkoxy, -NH(C₁₋₆alkyl) substituted with 0-2 R₆, and -N(C₁₋₆alkyl)(C₁₋₆alkyl) where each C₁₋₆alkyl is independently substituted with 0-2 R₆;

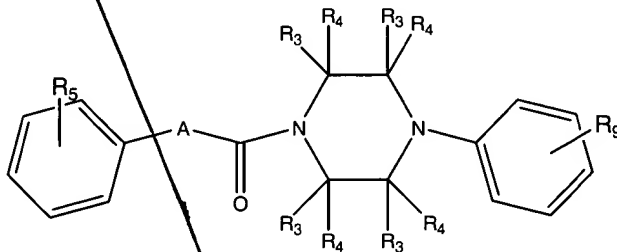
R₉ represents 0 to 2 substituents and is independently chosen at each occurrence from the group consisting of halogen, nitro, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, hydroxy, amino, C₁₋₆alkyl substituted with 0-2 R₆, C₂₋₆alkenyl substituted with 0-2 R₆, C₂₋₆alkynyl substituted with 0-2 R₆, and C₁₋₆alkoxy substituted with 0-2 R₆.

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R_{5A} is independently selected from the group consisting of halogen, cyano, nitro, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, hydroxy, amino, C₁₋₆ alkyl, C₁₋₆ alkoxy, -NH(C₁₋₆ alkyl), and -N(C₁₋₆ alkyl)(C₁₋₆ alkyl);

R_{9B} is independently selected from the group consisting of halogen, nitro, halo(C₁₋₆)alkoxy, hydroxy, amino, C₁₋₆ alkyl, and C₁₋₆ alkoxy; and

R₆ is independently selected at each occurrence the group consisting of halogen, hydroxy, C₁₋₄alkyl, C₁₋₄alkoxy, -NH(C₁₋₄ alkyl), and -N(C₁₋₄ alkyl)(C₁₋₄ alkyl).

27. (Amended) A compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

A is selected from the group consisting of a single bond, S, NR_A, NR_ACHR_B, CHR_BNR_A, -CR_A=CR_B-, and C₃H₄; where R_A and R_B are independently selected at each occurrence from the group consisting of hydrogen and alkyl;
each R₃ and R₄ is independently

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(a) selected from the group consisting of hydrogen; halogen; hydroxy; amino; cyano; nitro; -COOH; -CHO, optionally substituted alkyl; optionally substituted alkenyl; optionally substituted alkynyl; optionally substituted alkoxy; optionally substituted mono or dialkylamino; optionally substituted alkylthio; optionally substituted alkyl ketone; optionally substituted alkylester; optionally substituted alkylsulfinyl; optionally substituted alkylsulfonyl; optionally substituted mono- or di-alkylcarboxamide; optionally substituted $-S(O)_nNHalkyl$; optionally substituted $-S(O)_nN(alkyl)(alkyl)$; optionally substituted $-NHC(=O)alkyl$; optionally substituted $-NC(=O)(alkyl)(alkyl)$; optionally substituted $-NHS(O)_nalkyl$; optionally substituted $-NS(O)_n(alkyl)(alkyl)$; optionally substituted saturated or partially unsaturated heterocycle of from 5 to 8 atoms, which saturated or partially unsaturated heterocycle contains 1, 2, or 3 heteroatoms independently selected from N, O, and S; optionally substituted aryl having from 1 to 3 rings; and optionally substituted heteroaryl, said heteroaryl having from 1 to 3 rings, 5 to 8 ring members in each ring and, in at least one of said rings, from 1 to about 3 heteroatoms per ring independently selected from the group consisting of N, O, and S; or

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(b) joined to a R₃ or R₄ not attached to the same carbon to form an optionally substituted aryl ring; a saturated or partially unsaturated carbocyclic ring of from 5 to 8 members, which carbocyclic ring is optionally substituted; or a saturated, partially unsaturated, or aromatic heterocyclic ring of from 5 to 8 members, which heterocyclic ring is optionally substituted and contains 1, 2, or 3 heteroatoms independently selected from N, O, and S;

R₅ represents 0-3 substituents independently selected at each occurrence from the group consisting of cyano, nitro, haloalkyl, haloalkoxy, C₂₋₆ alkenyl substituted with 0-2 R₆, and C₂₋₆ alkynyl substituted with 0-2 R₆;

R₉ represents 0-3 substituents independently selected at each occurrence from the group consisting of bromo, haloalkyl, haloalkoxy, hydroxy, C₂₋₆ alkyl substituted with 0-2 R₆, C₂₋₆ alkenyl substituted with 0-2 R₆, C₂₋₆ alkynyl substituted with 0-2 R₆, and C₂₋₆ alkoxy;

R₆ is independently selected at each occurrence from the group consisting of halogen, hydroxy, cyano, alkyl, alkoxy, -S(O)_n(alkyl), haloalkyl, haloalkoxy, CO(alkyl), CONH(alkyl), CON(alkyl₁)(alkyl₂) where alkyl₁ and alkyl₂ may be joined to form a heterocycle of from 5 to 8 ring atoms and containing

1, 2, or 3 heteroatoms independently selected from N, O, and S, -XR₇, and Y;

X is independently selected at each occurrence from the group consisting of -CH₂-, -CHR₈-, -O-, -S(O)_n-, -NH-, -NR₈-, -C(=O)-, -C(=O)O-, -C(=O)NH-, -C(=O)NR₈-, -S(O)_nNH-, -S(O)_nNR₈-, NHC(=O)-, -NR₈C(=O)-, -NHS(O)_n-, and -NR₈S(O)_n-;

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R₇ and R₈ are independently selected at each occurrence from straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups, said straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups consisting of 3 to 8 carbon atoms, and containing zero or one or more double or triple bonds, each of which 3 to 8 carbon atoms is unsubstituted or substituted with one or more substituent(s) independently selected from oxo, hydroxy, halogen, amino, cyano, nitro, haloalkyl, haloalkoxy, -O(alkyl), -NH(alkyl), -N(alkyl)(alkyl), -NHC(O)(alkyl), -N(alkyl)C(O)(alkyl), -NHS(O)_n(alkyl), -S(O)_n(alkyl), -S(O)_nNH(alkyl), -S(O)_nN(alkyl₃)(alkyl₄) where alkyl₃ and alkyl₄ are optionally joined to form a heterocycle consisting of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms independently selected from N, O, and S, and Y';

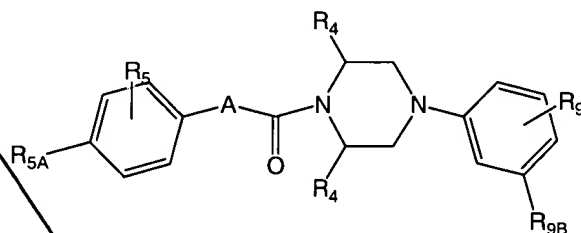
Y and Y' are independently selected at each occurrence from 3- to 8-membered carbocyclic or heterocyclic groups which are

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saturated, unsaturated, or aromatic, which are unsubstituted or substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, nitro, cyano, alkyl, alkoxy, haloalkyl, haloalkoxy, mono- or dialkylamino, and alkylthio; wherein said 3- to 8-membered heterocyclic groups contain one or more heteroatom(s) independently selected from N, O, and S; and

n is independently chosen at each occurrence from 0, 1, and 2.

30. (Amended) A compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

A is selected from the group consisting of NH, -CH=CH-, and CH₂NH;

R₄ is independently selected at each occurrence from hydrogen and C₁₋₄alkyl;

R₅ represents 0 to 2 substituents independently selected at each occurrence from the group consisting of halogen, cyano, nitro, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, amino, C₂₋₆alkenyl

substituted with 0-2 R₆, and C₂₋₆alkynyl substituted with 0-2 R₆;

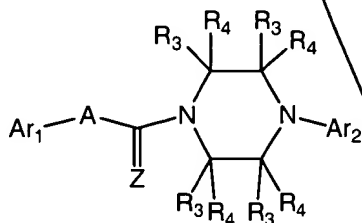
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R₉ represents 0 to 2 substituents and is independently selected at each occurrence from the group consisting of halogen, nitro, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, hydroxy, amino, C₁₋₆alkyl substituted with 0-2 R₆, C₂₋₆alkenyl substituted with 0-2 R₆, C₂₋₆alkynyl substituted with 0-2 R₆, and C₁₋₆alkoxy substituted with 0-2 R₆;

BS
R_{5A} is independently selected from the group consisting of halogen, cyano, nitro, trifluoromethyl, trifluoromethoxy, hydroxy, amino, C₁₋₆ alkyl, C₁₋₆ alkoxy, -NH(C₁₋₆ alkyl), and -N(C₁₋₆ alkyl)(C₁₋₆ alkyl);

R_{9B} is independently selected from the group consisting of trifluoromethoxy, hydroxy, C₂₋₆ alkyl, and C₂₋₆ alkoxy; and

R₆ is independently selected at each occurrence from the group consisting of halogen, hydroxy, C₁₋₄ alkyl, and C₁₋₄ alkoxy.

31. (Amended) A compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein the compound or pharmaceutically acceptable salt thereof

exhibits an EC50 or K_i of 1 micromolar or less in a standard assay of capsaicin receptor mediated calcium mobilization; and wherein

A is absent or is selected from the group consisting of O, S,

NR_A , $NR_ACR_BR_B'$, $CR_B R_B'NR_A$,

$-CR_A=CR_B-$, and C_3H_4 ; where R_A , R_B , and R_B' are independently selected at each occurrence from hydrogen and C_{1-6} alkyl;

Z is oxygen or sulfur;

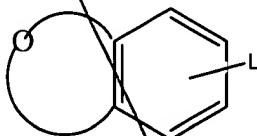
each R_3 and R_4 is independently

- (a) selected from the group consisting of hydrogen, halogen, cyano, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6} alkyl substituted with 0-2 R_6 , C_{2-6} alkenyl substituted with 0-2 R_6 ; C_{2-6} alkynyl substituted with 0-2 R_6 ; C_{1-6} alkoxy substituted with 0-2 R_6 , $-NH(C_{1-6}alkyl)$ substituted with 0-2 R_6 , $-N(C_{1-6}alkyl)(C_{1-6}alkyl)$ where each $C_{1-6}alkyl$ is independently substituted with 0-2 R_6 , $-XR_7$, and Y; or
- (b) joined to a R_3 or R_4 not attached to the same carbon to form an aryl ring substituted with 0-3 R_6 , a saturated or partially unsaturated carbocyclic ring of from 5 to 8 members, which carbocyclic ring is substituted with 0-2 R_6 , or a saturated, partially unsaturated, or aromatic heterocyclic ring of from 5 to 8 members, which heterocyclic ring is substituted with 0-2 R_6 and contains 1,

2, or 3 heteroatoms independently selected from N, O, and S;

Ar₁ is selected from the group consisting of:

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- (a) cyclohexyl, cyclopentyl, piperidinyl, piperazinyl, phenyl, pyrrolyl, furanyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, pyrimidyl, pyrazinyl, benzimidazolyl, naphthyl, indolyl, isoindolyl, benzofuranyl, isobenzofuranyl, benzo[b]thiophenyl, benz[d]isoxazolyl, quinolinyl, isoquinolinyl, cinnolinyl, quinazolinyl, and quinoxalinyl, each of which is optionally mono-, di-, or trisubstituted with R₅; and
- (b) bicyclic oxygen-containing groups of the formula:



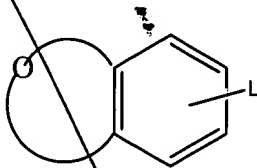
optionally mono-, di-, or trisubstituted with R₅, where L represents point of attachment and may be at any point on the benzene ring, and the oxygen-containing ring of the bicyclic oxygen-containing group consists of from 5 to 8 ring atoms, contains 1 or 2 oxygen atoms and remaining ring atoms are carbon;

Ar₂ is selected from the group consisting of:

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(a) cyclohexyl, cyclopentyl, piperidinyl, piperazinyl, pyrrolyl, furanyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, pyrimidyl, pyrazinyl, benzimidazolyl, naphthyl, indolyl, isoindolyl, benzofuranyl, isobenzofuranyl, benzo[b]thiophenyl, benz[d]isoxazolyl, quinolinyl, isoquinolinyl, cinnolinyl, quinazolinyl, and quinoxalinyl, each of which is optionally mono-, di-, or trisubstituted with R₅; and

(b) bicyclic oxygen-containing groups of the formula:



optionally mono-, di-, or trisubstituted with R₅, where L represents point of attachment and may be at any point on the benzene ring, and the oxygen-containing ring of the bicyclic oxygen-containing group consists of from 5 to 8 ring atoms, contains 1 or 2 oxygen atoms and remaining ring atoms are carbon;

R₅ is independently selected at each occurrence from the group consisting of halogen, nitro, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, hydroxy, amino, C₁₋₆alkyl substituted with 0-2 R₆, C₂₋₆alkenyl substituted with 0-2 R₆, C₂₋₆alkynyl substituted with 0-2 R₆, C₁₋₆alkoxy, and Y;

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R₆ is independently selected at each occurrence from the group consisting of halogen, hydroxy, cyano, C₁₋₄alkyl, C₁₋₄alkoxy, -S(O)_n(C₁₋₄alkyl), halo(C₁₋₄)alkyl, halo(C₁₋₄)alkoxy, CO(C₁₋₄alkyl), CONH(C₁₋₄alkyl), CON(C₁₋₄alkyl₁)(C₁₋₄alkyl₂) where alkyl₁ and alkyl₂ may be joined to form a heterocycle of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms independently selected from N, O, and S, -XR₇, and Y;

X is independently selected at each occurrence from the group consisting of -CH₂-, -CHR₈-, -O-, -S(O)_n-, -NH-, -NR₈-, -C(=O)-, -C(=O)O-, -C(=O)NH-, -C(=O)NR₈-, -S(O)_nNH-, -S(O)_nNR₈-, NHC(=O)-, -NR₈C(=O)-, -NHS(O)_n-, and -NR₈S(O)_n-;

R₇ and R₈ are independently selected at each occurrence from hydrogen, and straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups, said straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups consisting of 1 to 8 carbon atoms, and containing zero or one or more double or triple bonds, each of which 1 to 8 carbon atoms is unsubstituted or substituted with one or more substituent(s) independently selected from oxo, hydroxy, halogen, amino, cyano, nitro, haloalkyl, haloalkoxy, -O(C₁₋₄alkyl), -NH(C₁₋₄alkyl), -N(C₁₋₄alkyl)(C₁₋₄alkyl), -NHC(O)(C₁₋₄alkyl), -N(C₁₋₄alkyl)C(O)(C₁₋₄alkyl), -NHS(O)_n(C₁₋₄alkyl), -S(O)_n(C₁₋

$\text{alkyl})$, $-\text{S}(\text{O})_n\text{NH}(\text{C}_{1-4}\text{alkyl})$, $-\text{S}(\text{O})_n\text{N}(\text{C}_{1-4}\text{alkyl})_3(\text{C}_{1-4}\text{alkyl}_4)$

where $\text{C}_{1-4}\text{alkyl}_3$ and $\text{C}_{1-4}\text{alkyl}_4$ are optionally joined to form a heterocycle consisting of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms independently selected from N, O, and S, and Y';

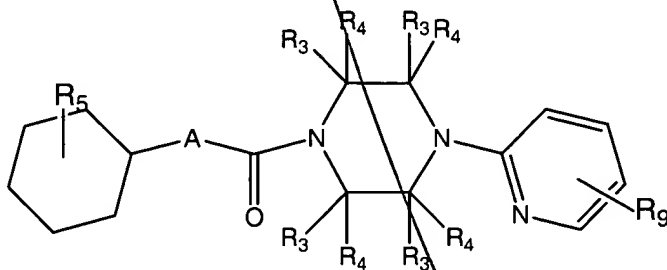
Y and Y' are independently selected at each occurrence from 3- to 8-membered carbocyclic or heterocyclic groups which are saturated, unsaturated, or aromatic, which may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, nitro, cyano, $\text{C}_{1-4}\text{alkyl}$, $\text{C}_{1-4}\text{alkoxy}$, $\text{halo}(\text{C}_{1-4})\text{alkyl}$, $\text{halo}(\text{C}_{1-4})\text{alkoxy}$, mono- or di(C_{1-4})alkylamino, and $\text{C}_{1-4}\text{alkylthio}$;

wherein said 3- to 8-membered heterocyclic groups contain one or more heteroatom(s) independently selected from N, O, and S;

and

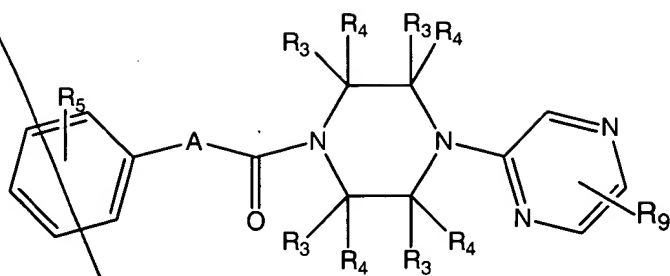
n is independently chosen at each occurrence from 0, 1, and 2.

32. (Amended) A compound of the Formula A, Formula B, Formula C, Formula D, Formula E, or Formula F:

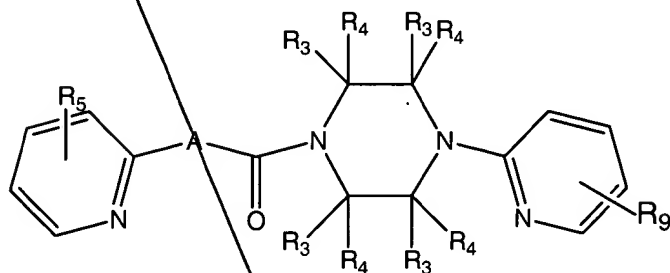


Formula A

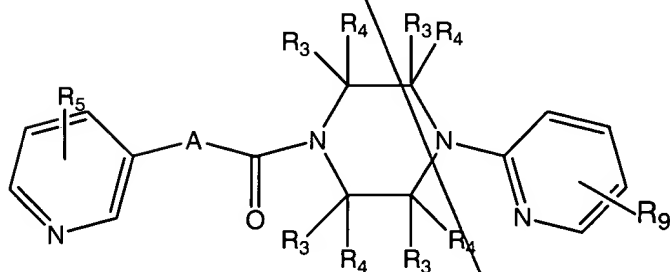
B



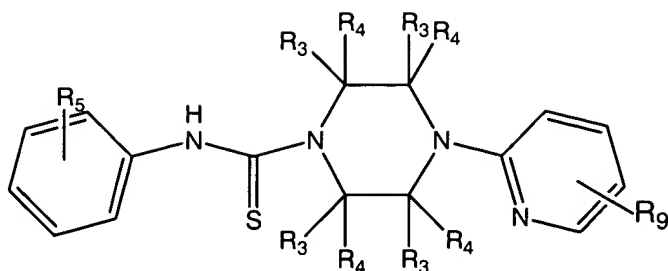
Formula B



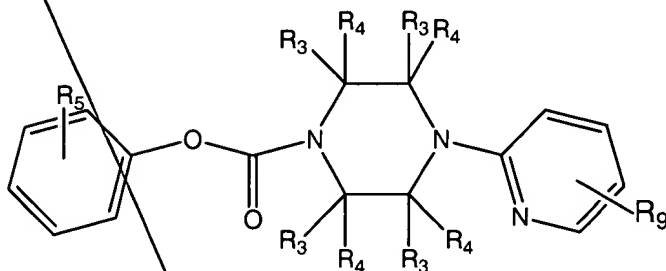
Formula C



Formula D



Formula E



Formula F

or a pharmaceutically acceptable salt of Formula A, Formula B, Formula C, Formula D, Formula E, or Formula F, wherein A represents NH or O;

each R₃ and R₄ is independently

- (a) selected from the group consisting of hydrogen, halogen, cyano, nitro, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, hydroxy, amino, C₁₋₆alkyl substituted with 0-2 R₆, C₂₋₆alkenyl substituted with 0-2 R₆; C₂₋₆alkynyl substituted with 0-2 R₆; C₁₋₆alkoxy substituted with 0-2 R₆, -NH(C₁₋₆alkyl) substituted

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B/S

with 0-2 R_6 , $-N(C_{1-6}alkyl)(C_{1-6}alkyl)$ where each $C_{1-6}alkyl$ is independently substituted with 0-2 R_6 , $-XR_7$, and Y ; or

(b) joined to a R_3 or R_4 not attached to the same carbon to form an aryl ring substituted with 0-3 R_6 , a saturated or partially unsaturated carbocyclic ring of from 5 to 8 members, which carbocyclic ring is substituted with 0-2 R_6 , or a saturated, partially unsaturated, or aromatic heterocyclic ring of from 5 to 8 members, which heterocyclic ring is substituted with 0-2 R_6 and contains 1, 2, or 3 heteroatoms independently selected from N, O, and S;

R_5 represents from 1 to 3 substituents independently selected at each occurrence from the group consisting of halogen, cyano, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, $C_{1-6}alkyl$ substituted with 0-2 R_6 , $C_{2-6}alkenyl$ substituted with 0-2 R_6 , $C_{2-6}alkynyl$ substituted with 0-2 R_6 , $C_{1-6}alkoxy$, $-NH(C_{1-6}alkyl)$ substituted with 0-2 R_6 , $-N(C_{1-6}alkyl)(C_{1-6}alkyl)$ where each $C_{1-6}alkyl$ is independently substituted with 0-2 R_6 , $-XR_7$, and Y ;

R_9 represents from 1 to 3 substituents independently selected at each occurrence from the group consisting of halogen, cyano, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, $C_{1-6}alkyl$ substituted with 0-2 R_6 , $C_{2-6}alkenyl$

substituted with 0-2 R₆, C₂₋₆alkynyl substituted with 0-2 R₆, C₁₋₆alkoxy substituted with 0-2 R₆, and Y;

R₆ is independently selected at each occurrence from the group consisting of halogen, hydroxy, cyano, C₁₋₄alkyl, C₁₋₄alkoxy, -S(O)_n(C₁₋₄alkyl), halo(C₁₋₄)alkyl, halo(C₁₋₄)alkoxy, CO(C₁₋₄alkyl), CONH(C₁₋₄alkyl), CON(C₁₋₄alkyl₁)(C₁₋₄alkyl₂) where alkyl₁ and alkyl₂ may be joined to form a heterocycle of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms independently selected from N, O, and S, -XR₇, and Y;

X is independently selected at each occurrence from the group consisting of -CH₂-, -CHR₈-, -O-, -S(O)_n-, -NH-, -NR₈-, -C(=O)-, -C(=O)O-, -C(=O)NH-, -C(=O)NR₈-, -S(O)_nNH-, -S(O)_nNR₈-, NHC(=O)-, -NR₈C(=O)-, -NHS(O)_n-, and -NR₈S(O)_n-;

R₇ and R₈ are independently selected at each occurrence from hydrogen, and straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups, said straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups consisting of 1 to 8 carbon atoms, and containing zero or one or more double or triple bonds, each of which 1 to 8 carbon atoms is unsubstituted or substituted with one or more substituent(s) independently selected from oxo, hydroxy, halogen, amino, cyano, nitro, haloalkyl, haloalkoxy, -O(C₁₋₄alkyl), -NH(C₁₋₄alkyl), -N(C₁₋₄alkyl)(C₁₋

B

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B/S
 ~~$C_{1-4}alkyl$), $-NHC(O)(C_{1-4}alkyl)$, $-N(C_{1-4}alkyl)C(O)(C_{1-4}alkyl)$, $-NHS(O)_n(C_{1-4}alkyl)$, $-S(O)_n(C_{1-4}alkyl)$, $-S(O)_nNH(C_{1-4}alkyl)$, $-S(O)_nN(C_{1-4}alkyl_3)(C_{1-4}alkyl_4)$ where $C_{1-4}alkyl_3$ and $C_{1-4}alkyl_4$ are optionally joined to form a heterocycle consisting of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms independently selected from N, O, and S, and Y';~~

Y and Y' are independently selected at each occurrence from 3- to 8-membered carbocyclic or heterocyclic groups which are saturated, unsaturated, or aromatic, which may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, nitro, cyano, $C_{1-4}alkyl$, $C_{1-4}alkoxy$, $halo(C_{1-4}alkyl)$, $halo(C_{1-4}alkoxy)$, mono- or di($C_{1-4}alkyl$)amino, and $C_{1-4}alkylthio$; wherein said 3- to 8-membered heterocyclic groups contain one or more heteroatom(s) independently selected from N, O, and S; and

n is independently chosen at each occurrence from 0, 1, and 2.

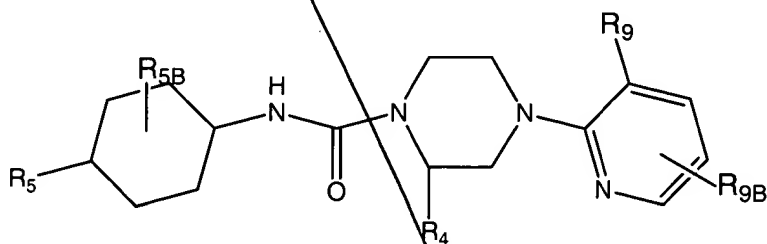
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37. (Amended) A compound or salt according to Claim 32, wherein:
A represents NH;
 R_3 represents hydrogen;

R₄ is independently chosen at each occurrence from hydrogen and methyl; and

R₅ represents from 1 to 3 substituents independently selected at each occurrence from the group consisting of halogen, cyano, nitro, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, hydroxy, amino, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆alkoxy, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)(C₁₋₆alkyl), and C₃₋₈ cycloalkyl; and

R₉ represents from 1 to 3 substituents independently selected at each occurrence from the group consisting of halogen, nitro, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, hydroxy, amino, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆alkoxy, and C₃₋₈ cycloalkyl.

38. (Amended) A compound or salt of the Formula A-1



Formula A-1

wherein

R₄ is hydrogen or methyl;

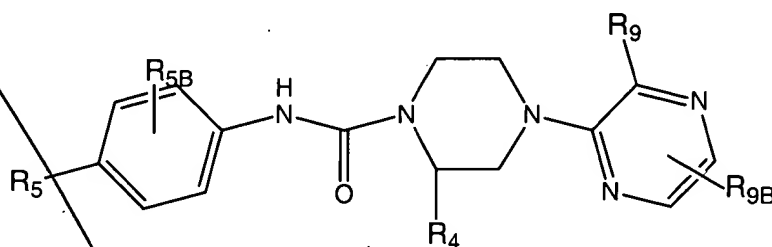
R₅ and R₉ are independently selected from the group consisting of halogen, cyano, nitro, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, hydroxy, amino, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋

B

~~alkoxy, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)(C₁₋₆alkyl), and C₃₋₈
cycloalkyl; and~~

~~R_{5B} and R_{9B} each represent from 0 to 2 substituents independently
selected at each occurrence from hydrogen, halogen, cyano,
nitro, halo(C₁₋₂)alkyl, halo(C₁₋₂)alkoxy, hydroxy, amino, C₁₋₃
alkyl, C₁₋₃alkoxy, -NH(C₁₋₃alkyl), and -N(C₁₋₆alkyl)(C₁₋₆
alkyl).~~

40. (Amended) A compound or salt of Formula B-1



Formula B-1

wherein

R₄ is hydrogen or methyl;

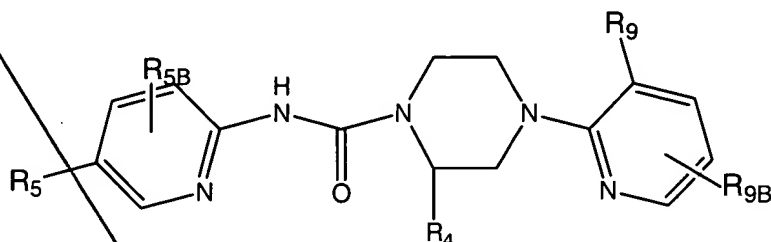
R₅ and R₉ are independently selected from the group consisting of
halogen, cyano, nitro, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy,
hydroxy, amino, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆
alkoxy, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)(C₁₋₆alkyl), and C₃₋₈
cycloalkyl; and

R_{5B} and R_{9B} each represent from 0 to 2 substituents independently
selected at each occurrence from hydrogen, halogen, cyano,
nitro, halo(C₁₋₂)alkyl, halo(C₁₋₂)alkoxy, hydroxy, amino, C₁₋

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B7

3alkyl, C₁₋₃alkoxy, -NH(C₁₋₃alkyl), and -N(C₁₋₆alkyl)(C₁₋₆alkyl).

42. (Amended) A compound or salt of Formula C-1



Formula C-1

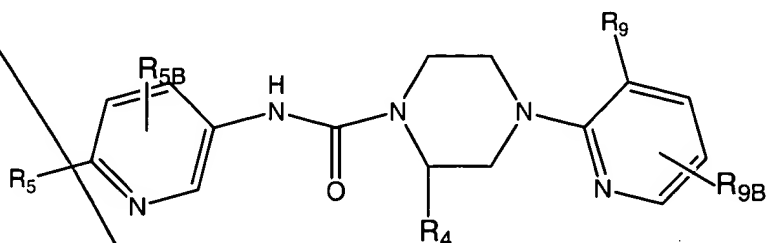
wherein:

R₄ is hydrogen or methyl;

R₅ and R₉ are independently selected from the group consisting of halogen, cyano, nitro, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, hydroxy, amino, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆alkoxy, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)(C₁₋₆alkyl), and C₃₋₈cycloalkyl; and

R_{5B} and R_{9B} each represent from 0 to 2 substituents independently selected at each occurrence from hydrogen, halogen, cyano, nitro, halo(C₁₋₂)alkyl, halo(C₁₋₂)alkoxy, hydroxy, amino, C₁₋₃alkyl, C₁₋₃alkoxy, -NH(C₁₋₃alkyl), and -N(C₁₋₆alkyl)(C₁₋₆alkyl).

44. (Amended) A compound or salt [according to Claim 37]
of Formula D-1



Formula D-1

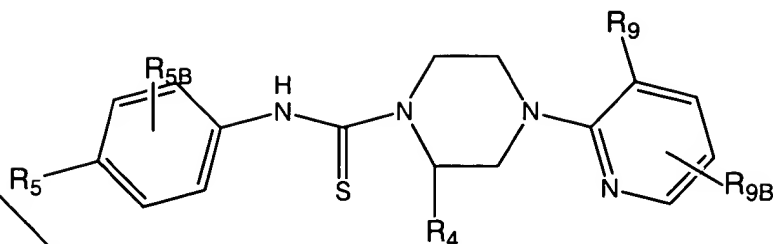
B9
wherein:

R₅ is selected from the group consisting of halogen, cyano, nitro, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, hydroxy, amino, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆alkoxy, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)(C₁₋₆alkyl), and C₃₋₈ cycloalkyl;

R₉ is selected from the group consisting of halogen, cyano, nitro, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, hydroxy, amino, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆alkoxy, and C₃₋₈ cycloalkyl; and

R_{5B} and R_{9B} each represent from 0 to 2 substituents independently selected at each occurrence from hydrogen, halogen, cyano, nitro, halo(C₁₋₂)alkyl, halo(C₁₋₂)alkoxy, hydroxy, amino, C₁₋₃alkyl, C₁₋₃alkoxy, -NH(C₁₋₃alkyl), and -N(C₁₋₆alkyl)(C₁₋₆alkyl).

B10
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C1
46. (Amended) A compound or salt of Formula E-1



Formula E-1

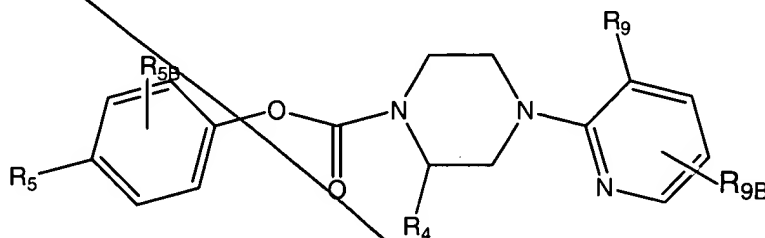
wherein:

R₄ is hydrogen or methyl;

R₅ and R₉ are independently selected from the group consisting of halogen, cyano, nitro, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, hydroxy, amino, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆alkoxy, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)(C₁₋₆alkyl), and C₃₋₈cycloalkyl; and

R_{5B} and R_{9B} each represent from 0 to 2 substituents independently selected at each occurrence from hydrogen, halogen, cyano, nitro, halo(C₁₋₂)alkyl, halo(C₁₋₂)alkoxy, hydroxy, amino, C₁₋₃alkyl, C₁₋₃alkoxy, -NH(C₁₋₃alkyl), and -N(C₁₋₆alkyl)(C₁₋₆alkyl).

48. (Amended) A compound of salt of Formula F-1



Formula F-1

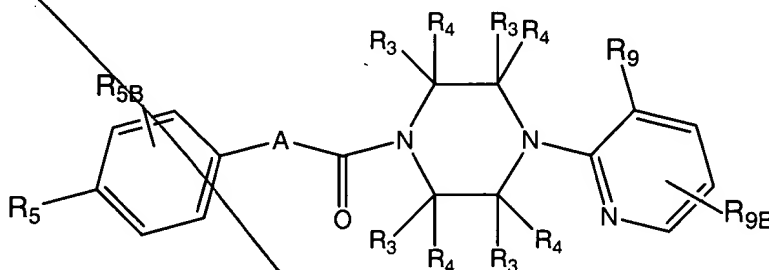
wherein:

R₄ is hydrogen or methyl;

R₅ and R₉ are independently selected from the group consisting of halogen, cyano, nitro, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, hydroxy, amino, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆alkoxy, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)(C₁₋₆alkyl), and C₃₋₈cycloalkyl; and

R_{5B} and R_{9B} each represent from 0 to 2 substituents independently selected at each occurrence from hydrogen, halogen, cyano, nitro, halo(C₁₋₂)alkyl, halo(C₁₋₂)alkoxy, hydroxy, amino, C₁₋₃alkyl, C₁₋₃alkoxy, -NH(C₁₋₃alkyl), and -N(C₁₋₆alkyl)(C₁₋₆alkyl).

50. (Amended) A compound of the Formula:



or a pharmaceutically acceptable salt thereof, wherein:

A is absent or is selected from the group consisting of O, S, NR_A, CR_BR_{B'}, NR_ACR_BR_{B'}, CR_BR_{B'}NR_A, -CR_A=CR_B-, and C₃H₄; where

R_A, R_B, and R_B' are independently selected at each occurrence from hydrogen and C₁₋₆ alkyl;

each R₃ and R₄ is independently

(a) selected from the group consisting of hydrogen, halogen, cyano, nitro, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, hydroxy, amino, C₁₋₆alkyl substituted with 0-2 R₆, C₂₋₆alkenyl substituted with 0-2 R₆; C₂₋₆alkynyl substituted with 0-2 R₆; C₁₋₆alkoxy substituted with 0-2 R₆, -NH(C₁₋₆alkyl) substituted with 0-2 R₆, -N(C₁₋₆alkyl)(C₁₋₆alkyl) where each C₁₋₆alkyl is independently substituted with 0-2 R₆, -XR₇, and Y; or

(b) joined to a R₃ or R₄ not attached to the same carbon to form an aryl ring substituted with 0-3 R₆, a saturated or partially unsaturated carbocyclic ring of from 5 to 8 members, which carbocyclic ring is substituted with 0-2 R₆, or a saturated, partially unsaturated, or aromatic heterocyclic ring of from 5 to 8 members, which heterocyclic ring is substituted with 0-2 R₆ and contains 1, 2, or 3 heteroatoms independently selected from N, O, and S;

R₅ is selected from the group consisting of bromo, fluoro, iodo, halo(C₁₋₆)alkyl, halo(C₃₋₆)alkoxy, C₃₋₆alkyl substituted with 0-3 R₆, C₂₋₆alkenyl substituted with 0-3 R₆, C₂₋₆alkynyl substituted with 0-3 R₆, C₃₋₆alkoxy, (C₃₋₈cycloalkyl)C₁₋₄alkyl,

~~-NH(C₁₋₆alkyl) substituted with 0-2 R₆, -N(C₁₋₆alkyl)(C₁₋₆alkyl) where each C₁₋₆alkyl is substituted with 0-2 R₆, Y, -(C=O)Y, -(CH₂)Y, and -(CH(CN))Y;~~

~~R₉ is selected from the group consisting of halogen, cyano, -N(SO₂C₁₋₆alkyl)(SO₂C₁₋₆alkyl), -SO₂NH₂, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, C₁₋₆alkyl substituted with 0-2 R₆, C₂₋₆alkenyl substituted with 0-2 R₆, C₂₋₆alkynyl substituted with 0-2 R₆, and C₁₋₆alkoxy substituted with 0-2 R₆;~~

~~R_{5B} represents from 0 to 2 substituents independently selected at each occurrence from the group consisting of~~

~~(a) halogen, cyano, nitro, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, hydroxy, amino, C₁₋₆alkyl substituted with 0-2 R₆, (C₃₋₈cycloalkyl)C₁₋₄alkyl substituted with 0-2 R₆, C₂₋₆alkenyl substituted with 0-2 R₆, C₂₋₆alkynyl substituted with 0-2 R₆, C₁₋₆alkoxy, -NH(C₁₋₆alkyl) substituted with 0-2 R₆, -N(C₁₋₆alkyl)(C₁₋₆alkyl) where each C₁₋₆alkyl is independently substituted with 0-2 R₆, and Y; and~~

~~(b) groups that are joined to R₅ to form a C₃₋₈cycloalkyl group or a saturated or partially unsaturated heterocycle, each of which is optionally substituted by from 1 to 5 substituents independently chosen from cyano, halogen, hydroxy, C₁₋₄alkyl, C₁₋₄alkoxy, -NH(C₁₋₄alkyl), -N(C₁₋₄alkyl)(C₁₋₄alkyl), halo(C₁₋₄)alkyl, and halo(C₁₋₄)alkoxy, wherein the saturated or partially unsaturated heterocycle contains from~~

B

4 to 8 ring atoms of which 1, 2, or 3 are heteroatoms
independently selected from N, O, and S;

Sub C1
R_{9B} represents from 0 to 2 substituents independently selected at
each occurrence from halogen, cyano, nitro, halo(C₁₋₆)alkyl,
halo(C₁₋₆)alkoxy, hydroxy, amino, C₁₋₆alkyl substituted with
0-2 R₆, (C₃₋₈cycloalkyl)C₁₋₄alkyl substituted with 0-2 R₆, C₂₋₆
alkenyl substituted with 0-2 R₆, C₂₋₆alkynyl substituted
with 0-2 R₆, C₁₋₆alkoxy substituted with 0-2 R₆, and Y;

81/2
R₆ is independently selected at each occurrence from the group
consisting of cyano, halogen, hydroxy, C₁₋₄alkyl, C₁₋₄alkoxy,
-S(O)_n(C₁₋₄alkyl), halo(C₁₋₄)alkyl, halo(C₁₋₄)alkoxy, CO(C₁₋₄
alkyl), CONH(C₁₋₄alkyl), CON(C₁₋₄alkyl₁)(C₁₋₄alkyl₂) where
alkyl₁ and alkyl₂ may be joined to form a heterocycle of
from 5 to 8 ring atoms and containing 1, 2, or 3
heteroatoms independently selected from N, O, and S, -XR₇,
and Y;

X is independently selected at each occurrence from the group
consisting of -CH₂-, -CHR₈-, -O-, -S(O)_n-, -NH-, -NR₈-, -
C(=O)-, -C(=O)NH-, -C(=O)NR₈-, -S(O)_nNH-, -S(O)_nNR₈-,
NHC(=O)-, -NR₈C(=O)-, -NHS(O)_n-, and -NR₈S(O)_n-;

R₇ and R₈ are independently selected at each occurrence from
hydrogen, and straight, branched, and cyclic alkyl groups,
and (cycloalkyl)alkyl groups, said straight, branched, and
cyclic alkyl groups, and (cycloalkyl)alkyl groups

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C1
B/2

consisting of 1 to 8 carbon atoms, and containing zero or one or more double or triple bonds, each of which 1 to 8 carbon atoms may be further substituted with one or more substituent(s) independently selected from oxo, hydroxy, halogen, amino, cyano, nitro, haloalkyl, haloalkoxy, $-O(C_{1-4}alkyl)$, $NH(C_{1-4}alkyl)$, $-N(C_{1-4}alkyl)(C_{1-4}alkyl)$, $-NHC(O)(C_{1-4}alkyl)$, $-N(C_{1-4}alkyl)C(O)(C_{1-4}alkyl)$, $-NHS(O)_n(C_{1-4}alkyl)$, $-S(O)_n(C_{1-4}alkyl)$, $-S(O)_nNH(C_{1-4}alkyl)$, $-S(O)_nN(C_{1-4}alkyl_3)(C_{1-4}alkyl_4)$ where $C_{1-4}alkyl_3$ and $C_{1-4}alkyl_4$ are optionally joined to form a heterocycle consisting of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms independently selected from N, O, and S, and Y';

Y and Y' are independently selected at each occurrence from 3- to 8-membered carbocyclic or heterocyclic groups which are saturated, unsaturated, or aromatic, which may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, nitro, cyano, $C_{1-4}alkyl$, $C_{1-4}alkoxy$, $halo(C_{1-4})alkyl$, $halo(C_{1-4})alkoxy$, mono- or di(C_{1-4})alkylamino, and $C_{1-4}alkylthio$; wherein said 3- to 8-membered heterocyclic groups contain one or more heteroatom(s) independently selected from N, O, and S; and

n is independently chosen at each occurrence from 0, 1, and 2.

59. (Amended) A compound or salt according to Claim 58
wherein:

*B13
Sub
C1* R₉ is selected from the group consisting of halogen, cyano, -
N(SO₂CH₃)₂, -SO₂NH₂,
halo(C₁₋₃)alkyl, and C₁₋₃alkoxy.

62. (Amended) A compound or salt according to Claim 57,
wherein:

*B14
Sub
C1* R₉ is selected from the group consisting of halogen, cyano, -
N(SO₂CH₃)₂, -SO₂NH₂,
halo(C₁₋₃)alkyl, and C₁₋₃alkoxy

R_{5B} represents 0 or 1 substituents chosen from halogen, cyano,
nitro, halo(C₁₋₂)alkyl,
halo(C₁₋₂)alkoxy, amino, C₁₋₄alkyl, and C₁₋₂alkoxy; and

R_{9B} represents 0 or 1 substituents chosen from halogen, cyano,
nitro, halo(C₁₋₂)alkyl,
C₁₋₂alkyl, and C₁₋₂alkoxy.

63. (Amended) A compound or salt according to Claim 57,
wherein:

R₅ is selected from the group consisting of bromo, fluoro, iodo,
halo(C₁₋₆)alkyl, halo(C₃₋₆)alkoxy, C₃₋₆alkyl substituted with
0-3 R₆, C₂₋₆alkenyl substituted with 0-3 R₆, Y, -(C=O)Y,

~~-(CH₂)Y, and -(CH(CN))Y;~~

~~R₉ is selected from the group consisting of halogen, cyano, -~~

~~N(SO₂CH₃)₂, -SO₂NH₂,~~

~~halo(C₁₋₂)alkyl, and C₁₋₃alkoxy;~~

~~R_{5B} represents 0 or 1 substituents chosen from halogen, cyano,~~

~~nitro, halo(C₁₋₂)alkyl,~~

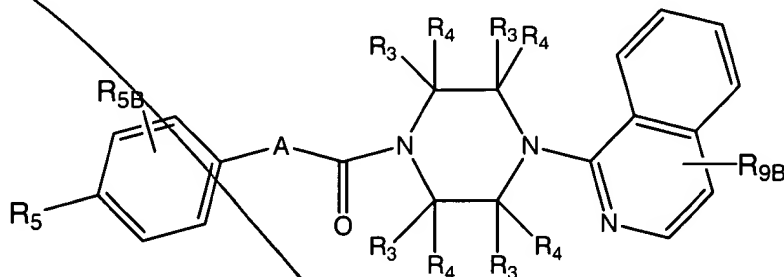
~~halo(C₁₋₂)alkoxy, amino, C₁₋₄alkyl, and C₁₋₂alkoxy; and~~

~~R_{9B} represents 0 or 1 substituents chosen from halogen, cyano,~~

~~nitro, halo(C₁₋₂)alkyl,~~

~~C₁₋₂alkyl, and C₁₋₂alkoxy.~~

161. (Amended) A compound of the Formula:



~~or a pharmaceutically acceptable salt thereof, wherein:~~

~~A is absent or is selected from the group consisting of O, S,~~

~~NR_A, CR_BR_{B'}, NR_ACR_BR_{B'}, CR_BR_{B'}NR_A, -CR_A=CR_B-, and C₃H₄; where~~

~~R_A, R_B, and R_{B'} are independently selected at each~~

~~occurrence from hydrogen and C₁₋₆ alkyl;~~

R₃ and R₄ are independently chosen at each occurrence from the group consisting of hydrogen, halogen, cyano, nitro, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, hydroxy, amino, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆alkoxy, -NH(C₁₋₆alkyl), and -N(C₁₋₆alkyl)(C₁₋₆alkyl);

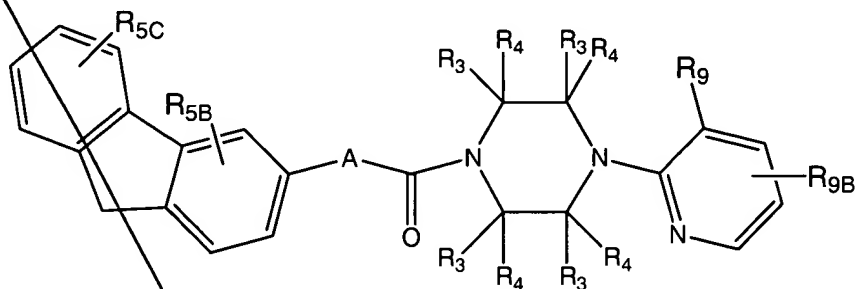
R₅ is selected from the group consisting of halogen, halo(C₁₋₆)alkyl, C₃₋₆alkyl substituted with 0-3 R₆, C₂₋₆alkenyl substituted with 0-3 R₆, (C₃₋₈cycloalkyl)C₁₋₄alkyl substituted with 0-3 R₆, and Y;

B/S
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C1
R_{5B} and R_{9B} each represent from 0 to 2 substituents and are independently chosen from halogen, cyano, nitro, halo(C₁₋₂)alkyl, halo(C₁₋₂)alkoxy, amino, C₁₋₄alkyl, and C₁₋₂alkoxy;

R₆ is independently selected at each occurrence from the group consisting of cyano, halogen, hydroxy, C₁₋₄alkyl, C₁₋₄alkoxy, -NH(C₁₋₄alkyl), -N(C₁₋₄alkyl)(C₁₋₄alkyl) and Y;

Y is independently selected at each occurrence from C₃₋₈ cycloalkyl, piperidinyl, piperazinyl, tetrahydropyranyl, dihydropyranyl, morpholinyl, thiomorpholinyl, phenyl, pyridyl, pyrazinyl, pyrimidinyl, thiazolyl, thienyl, and imidazolyl, each of which may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, nitro, cyano, C₁₋₄alkyl, C₁₋₄alkoxy, halo(C₁₋₄)alkyl, halo(C₁₋₄)alkoxy, mono- or di(C₁₋₄)alkylamino, and C₁₋₄alkylthio.

169. (Amended) A compound of the Formula:



or a pharmaceutically acceptable salt thereof, wherein:

A is absent or is selected from the group consisting of O, S, NR_A, CR_BR_{B'}, NR_ACR_BR_{B'}, CR_BR_{B'}NR_A, -CR_A=CR_B-, and C₃H₄; where R_A, R_B, and R_{B'} are independently selected at each occurrence from hydrogen and C₁₋₆ alkyl;

R₃ and R₄ are independently chosen at each occurrence from the group consisting of hydrogen, halogen, cyano, nitro, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, hydroxy, amino, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆alkoxy, -NH(C₁₋₆alkyl), and -N(C₁₋₆alkyl)(C₁₋₆alkyl);

R_{5B}, R_{5C}, and R_{9B} each represent from 0 to 2 substituents and are independently chosen from halogen, cyano, nitro, halo(C₁₋₂)alkyl, halo(C₁₋₂)alkoxy, amino, C₁₋₄alkyl, and C₁₋₂alkoxy; and

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R₉ is selected from the group consisting of halogen, cyano, -N(SO₂CH₃)₂, -SO₂NH₂, halo(C₁₋₃)alkyl, C₁₋₃alkoxy, -NH(C₁₋₃alkyl), and -N(C₁₋₃alkyl)(C₁₋₃alkyl).

Please add new claims 199-209:

199. (New) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound or salt according to claim 4.

B/R

200. (New) A package comprising a pharmaceutical composition of claim 199 in a container and further comprising indicia comprising instructions for using the composition to alleviate pain.

Sub
Cl

201. (New) A package comprising a pharmaceutical composition of claim 199 in a container and further comprising indicia comprising instructions for using the composition to alleviate symptoms of exposure to capsaicin or tear gas.

202. (New) A compound or salt of claim 4 wherein, in an *in vitro* assay of capsaicin receptor antagonism, the compound or salt exhibits capsaicin receptor antagonist activity, but in an *in vitro* assay of capsaicin receptor agonism the compound does not exhibit detectable agonist activity.

203. (New) A compound or salt of claim 4 wherein a dose of the compound or salt that is twice the minimum dose sufficient to provide analgesia in an animal model for determining pain relief does not produce sedation in an animal model assay of sedation.

B17
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C1
204. (New) 4-(3-Chloro-2-pyridinyl)-N-[4-(isopropyl)phenyl]-1-piperazinecarboxamide or a pharmaceutically acceptable salt thereof.

205. (New) (2R)-N-(4-tert-butylphenyl)-4-[3-(dimethylamino)pyridin-2-yl]-2-methylpiperazine-1-carboxamide or a pharmaceutically acceptable salt thereof.

206. (New) (2R)-4-[3-(dimethylamino)pyridin-2-yl]-2-methyl-N-[4-(trifluoromethyl)phenyl]piperazine-1-carboxamide or a pharmaceutically acceptable salt thereof.

207. (New) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound or salt according to claim 27.

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C1
B17
208. (New) A compound or salt of claim 27 wherein, in an in vitro assay of capsaicin receptor antagonism, the compound or salt exhibits capsaicin receptor antagonist activity, but in an in vitro assay of capsaicin receptor agonism the compound does not exhibit detectable agonist activity.

209. (New) A compound or salt of claim 27 wherein a dose of the compound or salt that is twice the minimum dose sufficient to provide analgesia in an animal model for determining pain relief does not produce sedation in an animal model assay of sedation.

210. (New) A package comprising a pharmaceutical composition of claim 207 in a container and further comprising indicia comprising instructions for using the composition to alleviate pain.

211. (New) A package comprising a pharmaceutical composition of claim 207 in a container and further comprising indicia comprising instructions for using the composition to alleviate symptoms of exposure to capsaicin or tear gas.